TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS: NONE

8EHQ-0702 15172

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2002 JUL 30 AM 11:17

1.0 SUBMISSION TYPE

☐ 8(d) **XX 8(e)** ☐ FYI ☐ 4 ☐ OTHER: Specify_____

XX- Initial Submission - Follow-up Submission ☐ Final Report Submission

Previous EPA Submission Number or Title if update or follow-up: Docket Number, if any: #

☐ continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED
(may be required for 8(e): optional for §4, 8(d) & FYI)

X- YES ☐ NO

2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID
7106 4575 1292 0338 1453
02-2-15

2.3 FOR EPA USE ONLY

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY

Reported Chemical Name (specify nomenclature if other than CAS name):
P-NITROTOLUENE

CAS# : 99-99-0

Purity ___%

X- Single Ingredient

☐ Commercial/Tech Grade

☐ Mixture *Trade Name* P-NITROTOLUENE *Common Name:*

CAS Number *NAME* *% WEIGHT*

Other chemical(s) present
in tested mixture

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4.0 REPORT/STUDY TITLE

Reproduction/Developmental Toxicity Screening Test with Oral Administration in Rats (draft report)

☐ continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]
HEALTH EFFECTS (HE): X ENVIRONMENTAL EFFECTS (EE):_____ ENVIRONMENTAL FATE (EF):_____

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)

STUDY TYPE: DTOX SUBJECT ORGANISM (HE, EE) RATS ROUTE OF EXPOSURE (HE only):__ VEHICLE OF EXPOSURE (HE only)_

Other: *Other:* *Other:* *Other:*

6.0 REPORT/STUDY INFORMATION ☐ Study is GLP

Laboratory Bayer Toxicology Report/Study Date : 07/15/2002re

Source of Data/Study Sponsor (if different than submitter) _____ Number of pages _-

☐ continuation sheet attached

7.0 SUBMITTER INFORMATION

Janet M. Mostowy, Ph.D.
VP, Product Safety & Regulatory Affairs
Bayer Corporation - 100 Bayer Road, Pittsburgh, PA. 15205
Phone: 412-777-3490

Technical Contact: **SAME AS ABOVE** Phone: ( )_____

☐ continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS

This is a commercial product. Information will be made known on product literature

☐ continuation sheet attached

Submitter Signature: _____ **Date: 07/16 /02**

Contain NO CBI

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ML 60808

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9.0 CONTINUATION SHEET

Submitter Tracking Number/Internal ID

7106 4575 1292 0338 1453
02-2-15

Continuation of 2.1

Reporting is based on the histopathological findings and the reproductive effects observed in this study.

Abstract: Groups of 12 male and female Wistar rats were treated daily by gavage for two weeks before mating, during a 2-week mating period, during a 1-week re-mating period, during gestation, lactation, and up to the day before necropsy with p-nitrotoluene (99.8%) dissolved in polyethylene glycol 400 at doses of 0, 25, 100, and 400 mg/kg body weight. Males were necropsied on day 36 of the study and females were necropsied between day 4 to 6 p.p. F_1 pups were sacrificed between day 4 to 6 p.p. The general toxicity of the test compound to the parental animals was evaluated (including histopathology of testes, epididymides, accessory sexual glands, ovaries, mammae with mammillae, liver, spleen, kidneys, pituitary gland, and organs with macroscopic findings) as well as on effects on reproduction, including early postnatal development of F_1 pups. Salivation, after administration, occurred in all groups and both genders and was most probably caused by the vehicle. The increased incidence of this finding in the treatment groups was probably related to the offensive smell and/or gustatory component of the test substance.

After the start of treatment with p-nitrotoluene, at the 400 mg/kg dose level signs of severe systemic toxicity were observed in both genders which included piloerection, respiratory sounds, sunken flanks, increased water intake, increased urination, and reduced amount of feces. In the females, hypoactivity, alterations of gait, and an increased incidence of soft and light colored feces were also observed. The clinical symptoms occurred together with distinctly to severely decreased feed intake and severe body weight loss which resulted in the spontaneous death of one male and the sacrifice, in moribund condition, of 2 males and 5 females up to day 8 of the study. Another female in the 400 mg/kg dose group was sacrificed moribund on day 22 p.c. and revealed intrauterine death of its litter at necropsy.

Recovery was observed in both genders during the 2nd week of the premating period, but clinical symptoms, reduced feed intake, and reduced body weight gain reappeared in females in the 400 mg/kg dose group during gestation and lactation. Necropsy of the animals in the 400 mg/kg dose group revealed alterations of the gastrointestinal tract in sacrificed/died animals of both genders as well as single cases of alterations of the spleen and prenatal litter loss in females. Increased weight of the liver, spleen and to a slight degree the kidney was observed in the males in the 400 mg/kg dose group. Increased kidney and liver weight were also observed to a marginal or slight degree in males in the 100 mg/kg dose group. In females, only the spleen weight was increased at the 400 mg/kg dose level.

Histopathology revealed, in both genders, morphological evidence of increased turnover of erythrocytes in the spleen in the 100 and 400 mg/kg dose groups and iron pigment and variable glycogen content in the liver in the 400 mg/kg dose group. Histopathological findings of the kidney consisted of single cell necrosis of renal tubular epithelial in males in the 400 mg/kg dose group while lipofuscin pigment was seen in the renal proximal tubules in females together with vacuolation of tubules (only in sacrificed females). Debris was observed in the epididymides of animals in the 400 mg/kg dose group together with exfoliation of spermatids in a single male.

With respect to reproductive parameters, including early postnatal development, treatment-related effects on the course of birth and lactation behavior could not be completely excluded at the 400 mg/kg dose level. Furthermore, a decrease in the gestation index, increased prenatal loss, reduced litter size at birth, clinical symptoms in pups (no milk spot and hematomas), impaired pup weight up to day 4 p.p., and impaired viability index up to day 4 p.p occurred in the 400 mg/kg dose group. Pup weight at birth was also slightly reduced in the 100 mg/kg dose group.